Early implementation of continuous renal replacement therapy optimizes casualty evacuation for combat-related acute kidney injury

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BACKGROUND: The purpose of this report was to review the initial use and feasibility of continuous renal replacement therapy (CRRT) among combat casualties in a war zone. Although rapid evacuation to more advanced levels of care has emerged as the standard approach, life-threatening sequelae of acute kidney injury (AKI) can preclude safe patient evacuation. For the first time in US combat casualty care, a sustained, intensivist-led CRRT program was initiated during 2010 at an Air Force theater hospital.

METHODS: A prospective study of consecutive US service members (USSMs) who developed combat-related renal failure and underwent CRRT at the Craig Joint Theater Hospital was undertaken. Baseline patient characteristics, indications for CRRT, laboratory values, and outcomes were evaluated.

RESULTS: Nine USSMs were treated during 14-months. All were male, with a mean (SD) age of 28 (7) years and mean (SD) Injury Severity Score (ISS) of 34 (12). The dominant mechanism was blast injury (8 of 9), followed by gunshot wound (1 of 9). Most patients were Acute Kidney Injury Network (AKIN) 3 and all developed critical hyperkalemia (mean [SD], peak K^+ 6.4 [0.4]). The peak plasma creatinine ranged from 1.4 mg/dL to 4.2 mg/dL (mean [SD], 3.3 [0.9] mg/dL). Patients had a mean (SD) of 17.6 [8.1] hours of CRRT before evacuation to higher echelons of care. All USSMs survived to achieve safe evacuation from the combat zone to the regional trauma center in Landstuhl, Germany (Landstuhl Regional Medical Center). Three patients died of multiorgan failure at Landstuhl Regional Medical Center. Six patients survived to undergo additional treatment in the United States.

CONCLUSION: Intensivist-led CRRT is an effective therapeutic adjunct in the treatment of combat-related AKI. Provision of this extracorporeal therapy provides physiologic stabilization of casualties who might otherwise succumb to the sequelae of combat-related renal failure. These findings suggest that a self-sustaining CRRT program can be successfully implemented in combat support hospitals. (*J Trauma Acute Care Surg*. 2013;75: S210–S214. Copyright © 2013 by Lippincott Williams & Wilkins)

LEVEL OF EVIDENCE: Therapeutic study, level V.

KEY WORDS: CRRT; acute kidney injury; combat.

During the current conflict in Afghanistan, the medical infrastructure for combat support has made significant improvements in many areas. Advances in prehospital care, damage-control surgery, and rapid aeromedical evacuation between echelons of care have proven to be invaluable in influencing patient survival. With such rapid improvements, casualties are surviving the initial physiologic insult of injury and subsequently are at risk to develop early complications in the intensive care unit. As a consequence of the index mechanism of injury, the improvised explosive device, patients surviving the initial blast present with multisystem polytrauma. As a secondary effect of large soft tissue destruction, the early development of rhabdomyolysis and acute kidney injury (AKI) has been observed.[1]

Improvements in tactical combat casualty care and early resuscitation have fueled a new demand for early advanced critical care management options for severely wounded combat casualties. Early renal replacement therapy (RRT) was acknowledged by some as potentially lifesaving in many instances.[2,3] However, the incidence of early AKI resulting in severe, life-threatening electrolyte imbalance was undocumented in the early stages of the most recent conflicts. Therefore, it was generally felt to be insufficient to justify the establishment of far forward extracorporeal therapies such as continuous RRT (CRRT). Thus, the doctrine of initial stabilization and rapid transport to Level IV or V facilities where such advanced therapies could be used in a familiar environment became the standard practice.

Over time, calls from deployed trauma and critical care providers for such interventions among coalition troops began to mount, and a performance improvement review seemed to

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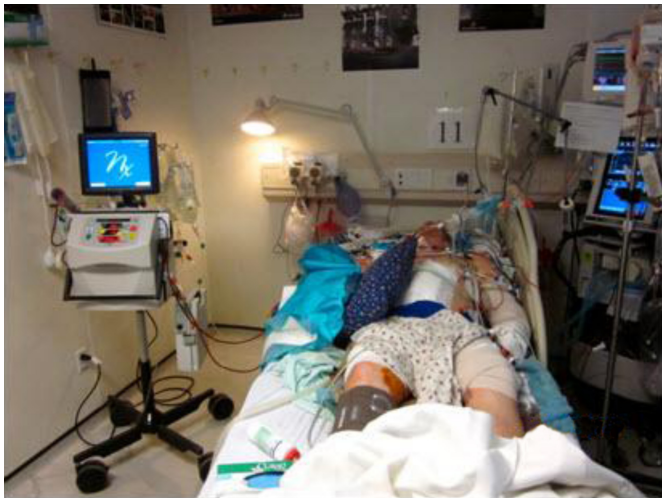

Figure 1. First patient treated with CRRT.

justify the added resources required to push RRT as far forward as hospital level (i.e., Role III) facilities. Significant unknowns still existed, however, including the incidence of early AKI, the underlying risks factors for the development of AKI, the appropriate indications for using RRT in-theater, and the logistical tail that would come with establishing such a capability. Thus, as this capability was established, the need for answers to these questions was anticipated, and data were collected prospectively to better understand the characteristics of early AKI in a combat environment and the potential benefits of CRRT availability in a Role III facility.

In anticipation for long-range strategic evacuation, a sustainable intervention to reverse AKI-related acid-base disorders, severe hyperkalemia, and metabolic disorders became apparent. Based on the mounting pressure and internal performance improvement initiatives, in the fall of 2010, RRT was permanently brought to a Role III facility in Afghanistan (Fig. 1). A local clinical practice guideline was established for the initiation and termination of CRRT. The purpose of this article was to review the feasibility of an established RRT program in support of combat casualties who developed trauma-related AKI. Here, we describe the first 14 months of experience with CRRT.

PATIENTS AND METHODS

A prospective observational series of consecutive US service members (USSMs) treated with CRRT at the Craig Joint Theater Hospital (CJTH–North Atlantic Treaty Organization Role III), Afghanistan was undertaken. Inclusion criteria included service members older than 18 years who developed severe AKI and, based on clinical assessment, required RRT. In each case, initiation of CRRT was based on the surgical intensivist's clinical decision. Severe kidney injury was a clinical decision based on Acute Kidney Injury Network (AKIN) criteria as well as potentially life-threatening acid-base disorders.[4] Study exclusion criteria included host-nation patients who may have undergone similar therapy and those younger than 18 years. The study period was from October 2010 through April 2012.

The NxStage System One (NXStage Medical, Lawrence, MA) was selected for use at the Role III facility. At the time of the device selection, there was not an assigned nephrologist at the facility. The surgical intensivist (author) was previously trained on the same system before deployment at the US Army Institute for Surgical Research, Texas, where an intensivist-led, intensive care unit (ICU) nurse–run CRRT program had been sustained since 2005.[5] This portable RRT platform is simple in design, based on its initial intent to market it for home use and has eliminated the need for operation by specialized dialysis technicians.[2] With menu-driven graphical user interface controls, volumetric balancing, simple button options, integrated cartridges, preformulated fluid replacement, and simple effluent drainage capability, it could be easily deployed to a fixed combat facility such as CJTH.

Our specific needs included the ability to perform continuous venonvenous hemofiltration or hemodialysis in short runs (8–18 hours) at relatively high doses (35–45 mL/kg/h) for electrolyte and metabolic control in preparation for long-range evacuation out of the combat zone.[2] Venous access was obtained using a dual-lumen 12 Fr to 14 Fr catheter (Mahurkar catheter, Mansfield, MA), preferentially in the internal jugular vein. Targeted blood flow rates were between 250 mL/min and 300 mL/min. All therapy fluids were delivered prefilter in a convective hemofiltration configuration (continuous venonvenous hemofiltration or hemodialysis). Anticoagulation was often dictated by the physiologic status of the patient and left to the discretion of the attending physician.

Baseline characteristics were obtained on all consecutively treated patients. This included age, sex, military service branch, mechanism of injury, Injury Severity Score (ISS), and indication for CRRT. The AKIN criteria were used to categorize and stage the degree of AKI.[4] Peak serum potassium (mmol/L), peak serum creatinine (mg/dL), and peak creatinine kinase (U/L) were also recorded. Rhabdomyolysis was defined as a serum creatinine kinase concentration of greater than 5,000 U/L.[6] CRRT dose (mg/kg/h) and total duration of therapy were recorded for each patient. Summary results for continuous variables are reported as means (SD). Continuous variables were compared using a two-tailed Student's t test with an $\alpha = 0.05$. Short-term outcomes at the Role III facility (mortality and safe-to-fly) were evaluated. Similarly, short-term outcomes at the Role IV facility (need for additional CRRT and mortality) were evaluated. With the use of Trauma and Injury Severity Score (TRISS) methodology,[7] predicted and observed survival were determined. All data were evaluated using STATA version 12 (College Station, TX). The data collection tool and project plan were reviewed and determined to be a performance improvement project by the Joint Combat Casualty Research Team. Our methods conform to the STROBE statement guidelines.[8]

RESULTS

From October 2010 through April 2012, a total of nine USSMs developed AKI and underwent CRRT. The majority of patients were US Army soldiers with a mean (SD) age of 28 (7) years (Table 1). The dominant mechanism of injury was blast (89%) with a mean (SD) ISS of 34 (12). The mean (SD) military ISS was slightly higher at 37 (21). Seven patients

TABLE 1. Baseline Characteristics

Patient	Year	Service	Age	MOI	ISS	mISS	Ps
1	2010	USA	33	Blast	17	17	0.94
2	2010	USMC	31	Blast	45	45	0.20
3	2011	USA	19	Blast	36	45	0.01
4	2011	USMC	24	Blast	57	75	0.06
5	2011	USA	25	Blast	38	43	0.78
6	2011	USA	40	Blast	22	29	0.97
7	2012	USA	34	GSW	33	38	0.35
8	2012	USA	24	Blast	27	27	0.96
9	2012	USA	21	Blast	27	43	0.93
Mean (SD)			28 (7)		34 (12)	37 (21)	0.58

mISS, military ISS; MOI, mechanism of injury; Ps, probability of survival; USA, US Army; USMC, US Marine Corps.

(78%) developed AKIN Stage 3 AKI, one (11%) developed Stage 2, and the final (11%) developed Stage 1 (Table 2).[4,9] The predicted probability of survival in this population was 0.58 based on TRISS methodology.[7,10]

Acid-base disorder with severe hyperkalemia was the most common indication for renal replacement. Validation for critical care evacuation to the Role IV facility mandated a stabilized with minimal risk of cardiac dysrhythmia. As such, all patients in this cohort required renal replacement in the theater of operations. Hyperkalemia was present in all patients with a mean (SD) initial serum K^+ of 6.2 (0.1) mmol/L. The mean (SD) peak serum creatinine was 3.3 (0.9) mg/dL. The index injury in this population was polytrauma with traumatic amputation. Eight of nine patients developed serum-diagnosed rhabdomyolysis. The peak serum creatinine kinase was 45,571 (40,036) U/L.

The mean (SD) prescriptive dose of CRRT was 54 (19) mL/kg per hour using varying combinations of 0 K^+ or 4 K^+ therapy fluid. The mean (SD) duration of therapy was 18 (8) hours, with a typical 4-hour to 6-hour preflight period off therapy. Three of the nine patients received regional anticoagulation during therapy. Hyperkalemia significantly improved in all patients with a preflight measurement

TABLE 2. Renal Failure Characteristics

Patient	AKIN Stage	Peak K^+, mmol/L	Peak Cr, mg/dL	Peak CK, U/L
1	3	6.2	4.2	6,644
2	3	6.5	3.3	76,200
3	3	5.7	4.1	7,157
4	3	6.1	4.2	147,000
5	3	7.2	4.1	51,180
6	3	6.3	3.4	61,680
7	3	6.6	2.6	21,108
8	1	6.4	1.4	3,808
9	2	6.2	2.4	35,370
Mean (SD)		6.4 (0.4)	3.3 (0.9)	45,571 (46,036)

Peak CK, peak serum creatinine kinase concentration; Peak Cr, peak serum creatinine concentration; Peak K^+, peak serum potassium concentration.

TABLE 3. CRRT Characteristics

Patient	pH		K^+, mmol/L		CRRT	Duration
	Before	After	Before	After	Dose*	h
1	7.34	7.35	6.2	4.4	67	15
2	7.43	7.34	6.4	4.3	82	26
3	7.22	7.36	5.7	3.7	67	30
4	7.01	7.43	6.3	5.1	29	11
5	7.31	7.34	6.5	2.9	68	15
6	7.26	7.41	6.3	4.3	36	21
7	7.28	7.25	6.1	4.2	50	21
8	7.38	7.39	6.5	4.6	40	3
9	7.31	7.38	6.2	4.6	33	16
Mean (SD)	7.28 (0.0)	7.36 (0.0)	6.2 (0.1)	4.2 (0.2)	53 (19)	18 (8)

*CRRT dose in milliliter per kilogram per hour.

of 4.2 (0.2) mmol/L ($p < 0.05$) (Table 3). Although the metabolic acidosis is multifactorial in these patients, there was a trend toward improvement by the end of treatment (pH 7.28 vs 7.36, $p = 0.15$).

None of the treated patients died in Afghanistan and were transported without incident by a critical care air transport team to the Level IV facility in Landstuhl, Germany. The mean transit time between intensive care units was 12 hours (7 hours in-flight plus 5 hours of ground time in Afghanistan and Germany). All patients remained in AKI requiring additional renal replacement at Landstuhl Regional Medical Center (LRMC). Three patients (33%) ultimately died of multiple-organ failure at LRMC. The six remaining patients were transferred, and four required additional renal replacement. One of six patients ultimately died of injuries. With a predicted mortality of 42%, actual observed mortality was 44%.

DISCUSSION

Combat trauma–associated renal failure was first described by Bywaters and Beall[11] during their experience caring for patients during the London bombings in 1941. The ability to intervene in these cases with RRT in an austere combat environment was first made possible a decade later by Teschan[12] during the Korean War. This capability was maintained during the Vietnam War,[13] although many believed that the incidence of early acute renal failure was reduced as more aggressive crystalloid resuscitation became commonplace.[2]

Early in Operation Iraqi Freedom, the USS Comfort provided dialysis support for three combat casualties; however, this capability was not maintained.[14] A hospital-based dialysis augmentation team was made available by Army doctrine to support theater RRT needs in the beginning of this current conflict but was never activated. Nonetheless, several case reports and case series addressing renal replacement appear throughout the medical literature. These include makeshift peritoneal dialysis and expeditionary arteriovenous dialysis.[3,14,15] Given the lack of formal resources, much of the care provided was directed at host-nation patients when evacuation was not possible. Although great effort and ingenuity was used to perform this therapy, no ground-based formal therapies were available for patient sustaining AKI during combat

operations. Potential explanations for this capability regression relative to previous conflicts include the increased emphasis on early and rapid long-range evacuation of even critically ill combat casualties and the lack of adequate data justifying the activation of such a team. By 2008, the critical care air transport community circulated reports of challenging and sometimes risky in-transit management of electrolyte and acid-base disorders. Critical care providers felt strongly that providing RRT before transport in select cases would be beneficial. (Lt. Col. Dr. Phil Mason, personal communication, September 2012). Our article establishes the feasibility of RRT in support of combat operations and safe strategic medical evacuation.

Our results demonstrate that RRT can be safely applied in an austere environment before long-range critical care transport. In many instances, this therapy enabled safe transport by reducing critically high K^+ levels. The ultimate outcome of the patients in our study approximated the expected mortality achieved in the optimal care environment of civilian facilities. The use of CRRT in this series was limited to trained attending physicians (surgical intensivists, nephrologists), all experienced in the prescription of RRT. In addition, all were cognizant of appropriate target goals of therapy to enable safe evacuation and transport. Technical support included ICU nurses or technicians with previous training in hemodialysis or CRRT. Much like other CRRT naïve programs, these nurses assumed responsibility for training a core group of ICU nurses to become proficient in initiating therapy, changing therapy fluids, trouble shooting alarms, changing filter sets, as well as terminating and appropriately returning circuit blood. In the few instances where technician support by ICU nurses were inadequate, management of the machine was performed by a nephrologist or surgical intensivist.

This particular Role III facility (CJTH) was situated as the regional air hub for strategic patient evacuation out of theater. At the time of the study, three additional Role III facilities existed throughout the area of combat operations. However, all were feeder facilities to the Role III (CJTH) where CRRT was made available. The sending facilities were all within 2 hours to 4 hours of air transport, permitting relatively safe movement of patients in renal failure. Furthermore, patient movement during this period was such that patients arriving at CJTH were 2 days to 3 days after injury, a period when AKI was typically observed. As CJTH was colocated at the major air hub for the country, outbound patient movement was subject to extensive long-range evacuation with limited medical resources among patients in renal failure (10–14 hours of transport times). Therefore, optimizing acid-base status and hemostasis in potentially uremic patients allowed for a safer critical care movement to the next echelon of care.[16]

With advances in RRT technology making it compact and user-friendly, such an approach is feasible and poses fewer technical risks relative to so-called field-expedient means of performing RRT.[3] As such, establishment of a CRRT program de novo in a previously naïve ICU setting can be performed with relative ease even in a combat hospital environment. The greatest need is the identification of a physician champion with previous CRRT experience and credentials in the appropriate subspecialty (critical care and/or nephrology) who can establish protocols, develop order sets, and coordinate logistics. Second, identification of ICU nurses with previous CRRT experience, who then could provide training to other staff members, proved critical in getting the program initiated. Perhaps, the greatest challenge, especially during modern combat operations, is the constant inevitable turnover of rotating physicians and nursing staff. Sustainment of a viable CRRT program in such conditions requires a corporate-level commitment with the deliberate assignment of qualified individuals. Such a commitment has been achieved at CJTH, and the program continues successfully more than 2 years after implementation.

Mortality remains historically high in this patient population.[17] Although the current joint theater trauma registry captures almost 400 data points per patient, there is not an organized filter to capture those developing an AKI or an easy way to determine a number of those who may have benefited from such therapy. In the civilian literature, AKI occurs in approximately 7% of all hospitalized patients and 36% to 67% of critically ill patients.[18] The epidemiology of AKI in the combat population is under active investigation. Of those factors related to the development of AKI, our patient population is unique in that the at-risk population is young with few, if any, comorbidities.

The nature of injury tends to be significant soft tissue destruction secondary to blast injury. Although the rhabdomyolysis is clinically distinct from a crush injury, it is unclear what risk factors led to their development of AKI. Of the hundreds of combat casualties that have sustained polytraumatic injuries after blast injury, very few progress toward AKI requiring renal replacement. Accurate volume assessment in these complex patients presents a daunting resuscitation challenge. One must balance underresuscitation and large insensible loss with overresuscitation and the risk of multicompartment syndromes and pulmonary injury. One final factor that may contribute to AKI in these patients is the time to evacuation, from point of injury to forward resuscitation and ultimately throughout our system to higher levels of critical care treatment.

This study demonstrates the feasibility and sustainability of an RRT asset for Level III facilities in future large-scale conflicts. Although every effort was made to collect data prospectively, some combat casualties with indications for early RRT were undoubtedly missed. Furthermore, decisions to initiate and terminate therapy were based on the intensivist's clinical decision rather than a predetermined protocol. Future approaches include education on the indications for early RRT and the ability to provide this therapy even in theater through the dissemination of a theaterwide clinical practice guideline on renal insufficiency in combat casualties. Second, our results do not include a significant population of patients with AKI cared for in our theater hospitals—host nation and local national combat casualties. As such, our results are based on a relatively small number of patients, limiting our ability to make more conclusive assertions regarding this therapy. Similarly, this study does not account for combat casualties who had RRT initiated at a Role IV or V facility. Although RRT has always been available at Role V facilities, it was not routinely available at LRMC, which has been the only Role IV facility in the most recent US conflicts. Like the evolution of RRT availability in Role III facilities, use of RRT at LRMC was limited by the lack of

perceived need for this capability until the demand for this therapy led to the necessary logistical and professional support. Although dialysis capability was initiated at the Role IV in 2006, CRRT was only realized within the last 2 years.

It is our opinion that with the severity of combat injuries now seen in our forward facilities, RRT should be made available in theater for future large-scale conflicts. Such a capability is likely to ensure safe transport for even our most critically injured service members. Future advances in the clinical science behind RRT will allow us to further refine our patient selection and intensity of therapy. Furthermore, technology advances in membrane and circuit design will increase the spectrum of therapeutic indications for extracorporeal therapy while lowering the risk of thromboembolic and other circuit-related complications. As hands-on experience with RRT and other extracorporeal therapies becomes integral to critical care fellowship training, ensuring this high level of care for our combat casualties in the future should be more straightforward from a staffing perspective as well.

Finally, although not reported in this study, CRRT was not restricted to USSMs during this period. As a significant portion of medical care is provided to host-nation military and civilian casualties, the decision to initiate and terminate therapy was determined by a multidisciplinary team of providers. In regions of complex political emergency care, ethical considerations of initiating and terminating such a therapy must be well thought out. In host countries that lack sophisticated medical care, medical rules of engagement and practical considerations must be well planned and discussed among the interdisciplinary team and host-nation liaisons. In cases where sophisticated medical care cannot be sustained in the host country because of lack of infrastructure or access to care, it may be prohibitive to initiate a potentially long-term therapy. Rational guidance includes initiation for a specified period based on the acute nature of the injury. Under the assumption that the renal injury is reversible based on the underlying mechanism, setting realistic goals of care early during the course of treatment mitigates more difficult decisions during a potentially protracted course. With the foresight of the inevitable next war, it is our hope that the data presented in this article as well as the clinical experience of those caring for these severely injured patients will prompt the development of systemwide clinical practice guideline.

AUTHORSHIP

D.Z. designed the study. All authors contributed to the data collection, analysis, and interpretation. D.Z., J.E., J.C., and K.K.C. prepared the manuscript, which was critically reviewed by C.B., T.B., and J.D.

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DISCLOSURE

The authors declare no conflicts of interest.

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